

Patient-Reported Outcomes with Selpercatinib in Patients with *RET*-driven cancers in the Phase 1/2 LIBRETTO-001 Trial

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Background and Objective

Background

- Selpercatinib** is a first-in-class, highly selective, and potent *RE*arranged during *Trans*fection (***RET***)-kinase inhibitor with central nervous system activity approved for multiple *RET*-activated tumor types¹
- The US FDA recognizes the meaningfulness of health-related quality of life (HRQoL) in oncology trials²
- HRQoL data (December 2019) from the single-arm phase 1/2 LIBRETTO-001 trial was previously described for *RET* fusion+ non-small cell lung cancer (NSCLC) and *RET*-mutant medullary thyroid cancer (MTC)^{3,4}
 - Clinically meaningful improvements with selpercatinib were found in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (QLQ-C30) subscales
- Updated HRQoL data (January 2023) is now available for NSCLC, MTC, as well as for *RET*-fusion+ thyroid cancer (TC) and *RET*-fusion+ tumor-agnostic (TA) populations

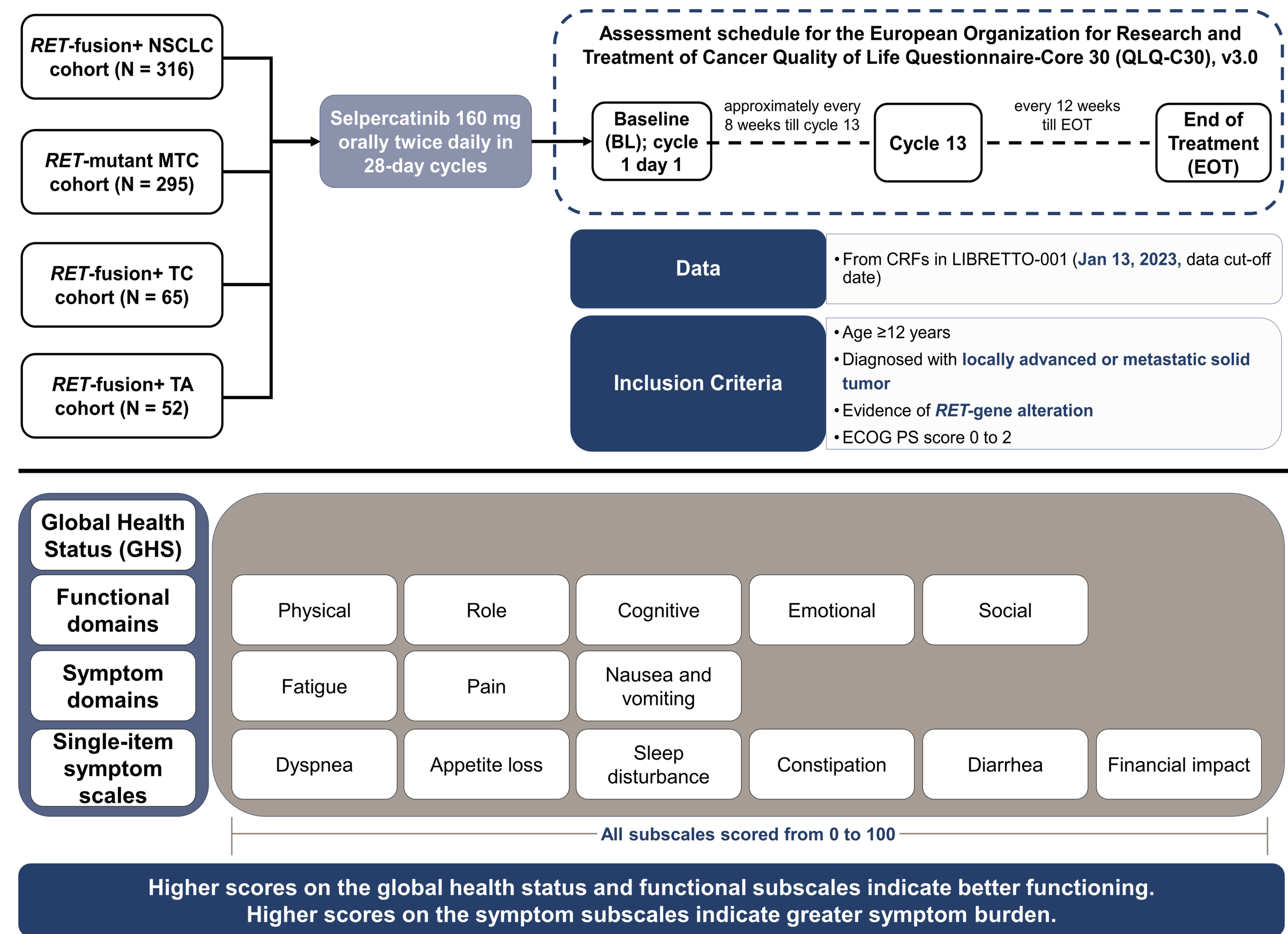
Objective

- To describe patient-reported symptoms and HRQoL in selpercatinib-treated patients with *RET*-activated cancers using a data cut-off date of January 2023

Methods

Study Design and Patient-Reported Outcome Assessment

- Retrospective analysis of data from the LIBRETTO-001 trial
- Patient-reported outcome (PRO) assessed with QLQ-C30⁵
 - A validated PRO measure translated to >100 languages and commonly used in oncology clinical trials



Number of patients who completed the QLQ-C30 may differ from the number of patients who received treatment. **Abbreviations:** BL – Baseline, CRF – Case Report Form, ECOG PS – Eastern Co-operative Oncology Group Performance Status, EOT – End of Treatment, MTC – Medullary Thyroid Cancer, NSCLC – Non-small Cell Lung Cancer, QLQ-C30 – European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30, *RET* – *RE*arranged during *Trans*fection, TA – Tumor-agnostic, TC – Thyroid Cancer

Outcomes and Statistical Analyses

Outcomes for all cohorts	Definition/ calculation	Statistical analysis
QLQ-C30 compliance	Total number of patients who completed QLQ-C30, divided by the total number of patients on treatment at each visit	Descriptive
Proportion of patients with improved, stable, or worsened status post-BL through cycle 37 for NSCLC and MTC, and through cycle 25 for TC and TA ^a	For symptom subscales: ⁶ Improved - ≥10-point decrease from BL Worsened - ≥10-point increase from BL Stable - being within 10 points from BL For other subscales: ⁶ Improved - ≥10-point increase from BL Worsened - ≥10-point decrease from BL Stable - being within 10 points from BL	Descriptive
Duration of improvement (DOI)	For symptom subscales: Time from the date of first improvement (10-point decrease from BL) to the date of first deterioration (≥10-point increase after the first improvement) For other subscales: Time from the date of first improvement (10-point increase from BL) to the date of first deterioration (≥10-point decrease after the first improvement)	Kaplan-Meier method. Reported as median (95% CI) number of months.
Time to first improvement (TTFI) ^b	For all subscales: Time from BL until the first improvement	
Time to first worsening (TTFW) ^c	For all subscales: Time from BL until the first worsening	

^a Cycle 37 and cycle 25 were chosen for this outcome since the median duration of follow-up for the primary endpoint of the trial (objective response rate), was approximately 37–39 months for NSCLC and MTC, and approximately 28 months for TC and TA. ^b If there is no first improvement, patients were censored at time to treatment discontinuation or last evaluable disease assessment, whichever occurs first. ^c If there is no first worsening, patients were censored at time to treatment discontinuation or last evaluable disease assessment, whichever occurs first. **Abbreviations:** BL – Baseline, CI – Confidence Interval, DOI – Duration of Improvement, MTC – Medullary Thyroid Cancer, NSCLC – Non-small Cell Lung Cancer, QLQ-C30 – European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30, TA – Tumor-agnostic, TC – Thyroid Cancer, TTFI – Time to First Improvement, TTFW – Time to First Worsening

Results

Patient Characteristics in the Cohorts

- At baseline, the NSCLC, MTC, TC, and TA cohorts had 316, 295, 65, and 52 patients, respectively

Parameter		NSCLC (N = 316)	MTC (N = 295)	TC (N = 65)	TA (N = 52)
Age in years, median (range)		61.0 (23–92)	58.0 (15–90)	59.0 (20–88)	54.0 (21–85)
Sex, n (%)	Male	133 (42.1)	180 (61.0)	32 (49.2)	25 (48.1)
	Female	183 (57.9)	115 (39.0)	33 (50.8)	27 (51.9)
ECOG PS, n (%)	0	115 (36.4)	111 (37.6)	25 (38.5)	16 (30.8)
	1	190 (60.1)	167 (56.6)	36 (55.4)	32 (61.5)
	2	11 (3.5)	17 (5.8)	4 (6.2)	4 (7.7)

Abbreviations: ECOG PS – Eastern Co-operative Oncology Group Performance Status, MTC – Medullary Thyroid Cancer, NSCLC – Non-small Cell Lung Cancer, TA – Tumor-agnostic, TC – Thyroid Cancer

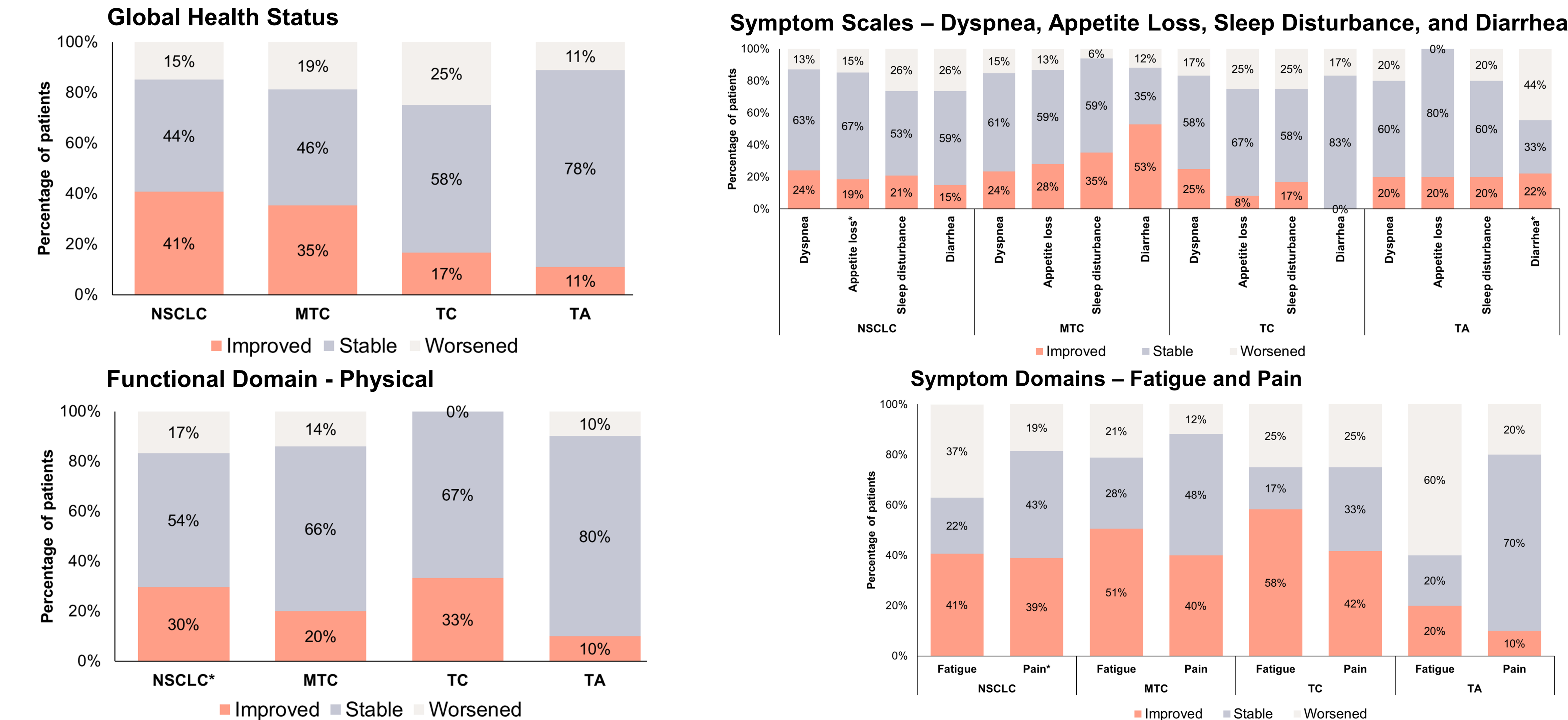
QLQ-C30 Compliance Rate

- In the NSCLC, MTC, TC, and TA cohorts, 63.3%, 70.8%, 76.9%, and 73.1% completed the baseline assessment; total compliance rate across all visits was 80.4%, 81.7%, 70.1%, and 85.2%, respectively

Results

Proportion of patients with improved, stable, or worsened status through cycle 37 (NSCLC and MTC) or cycle 25 (TC and TA)

- At least **75%, 56%, 83%, and 40%** of patients across all the cohorts reported **improved or stable QLQ-C30 scores for global health status, symptom scales, functional domains, and symptom domains**, respectively through cycle 37 or cycle 25 with selpercatinib use



Only clinically relevant parameters were reported. * After rounding off the percentages the total proportion may not be equal to 100%. **Abbreviations:** BL – Baseline, MTC – Medullary Thyroid Cancer, NSCLC – Non-small Cell Lung Cancer, QLQ-C30 – European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30, TA – Tumor-agnostic, TC – Thyroid Cancer

Selpercatinib demonstrated varied TTFI, DOI, and TTFW in QLQ-C30 subscales in all the cohorts

- TTFI ranged from 2.0 to 19.4 months across all cohorts** (shorter time to first event is associated with improved outcomes)
- DOI ranged from 1.9 to 28.2 months across all cohorts** (longer duration is associated with improved outcomes)
- TTFW ranged from 5.6 to 44.2 months across all cohorts** (shorter time to first event is associated with worsening outcomes)

Domain	Subscale	NSCLC			MTC			TC			TA		
		TTFI	DOI	TTFW	TTFI	DOI	TTFW	TTFI	DOI	TTFW	TTFI	DOI	TTFW
GHS		3.7 (2.1; 5.5)	5.6 (3.8; 8.3)	19.1 (11.3; 34.8)	5.5 (3.7; 7.3)	5.6 (3.7; 7.6)	30.4 (15.7; NE)	NE (3.9; NE)	2.8 (1.9; 5.8)	7.5 (3.7; 16.5)	2.0 (1.9; 5.3)	3.8 (2.8; 22.4)	NE (24.9; NE)
Functional domains	Physical	18.5 (7.4; NE)	5.6 (3.8; 7.6)	19.2 (13.8; 31.3)	NE (NE; NE)	9.2 (5.6; 18.4)	NE (25.1; NE)	NE (NE; NE)	6.9 (5.6; 34.3)	16.5 (7.4; 46.8)	4.2 (2.0; NE)	12.0 (3.7; NE)	NE (14.1; NE)
	Fatigue	3.7 (2.1; 3.9)	2.9 (2.1; 3.7)	9.2 (7.0; 11.3)	3.7 (2.1; 3.9)	3.6 (2.8; 3.7)	12.0 (9.1; 22.2)	5.5 (2.6; 22.3)	3.7 (2.0; 5.6)	5.6 (3.7; 10.2)	2.0 (1.9; 19.3)	12.0 (1.9; 25.5)	11.1 (3.9; NE)
Symptom domains	Pain	3.9 (2.1; 9.3)	5.6 (3.7; 6.2)	13.8 (9.5; 17.0)	3.9 (2.3; 11.1)	3.7 (2.8; 5.6)	16.5 (9.2; 22.1)	9.2 (3.7; NE)	3.7 (1.9; 4.7)	11.1 (3.7; 24.0)	3.7 (1.9; NE)	3.7 (1.9; NE)	24.9 (5.8; NE)
	Dyspnea	9.4 (3.7; NE)	5.6 (3.7; 7.6)	44.2 (33.2; NE)	NE (NE; NE)	5.6 (3.7; 12.0)	38.7 (19.5; NE)	16.8 (3.7; NE)	2.6 (1.9; 4.6)	NE (38.0; NE)	NE (NE; NE)	1.9 (1.6; NE)	20.5 (13.7; NE)
Single-item symptom scales	Appetite loss	NE (11.1; NE)	5.8 (4.6; 9.5)	27.5 (16.1; 42.4)	NE (NE; NE)	9.0 (5.6; 14.8)	42.8 (31.0; NE)	NE (NE; NE)	28.2 (3.7; NE)	13.8 (5.6; 36.1)	2.0 (1.9; NE)	NE (1.9; NE)	NE (30.4; NE)
	Sleep disturbance	19.4 (7.5; NE)	5.5 (3.7; 5.8)	31.1 (19.1; NE)	6.5 (3.8; 16.6)	4.1 (3.7; 5.6)	29.5 (19.8; 41.4)	11.7 (3.7; NE)	2.8 (1.9; 4.6)	19.4 (9.4; NE)	9.3 (3.7; NE)	5.8 (1.9; NE)	19.4 (13.7; NE)
	Diarrhea	NE (NE; NE)	2.8 (1.9; 5.6)	7.5 (5.8; 11.1)	3.3 (2.0; 5.5)	12.0 (7.4; 17.5)	NE (NE; NE)	NE (NE; NE)	1.9 (1.8; NE)	7.9 (3.8; 18.5)	NE (3.7; NE)	3.9 (1.8; 7.4)	11.1 (3.8; 26.0)

Values reported as median (95% CI) number of months, estimated with Kaplan-Meier method and Greenwood formula. Only clinically relevant parameters were reported. **Abbreviations:** DOI – Duration of Improvement, MTC – Medullary Thyroid Cancer, NE – Not Estimable, NSCLC – Non-small Cell Lung Cancer, QLQ-C30 – European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30, TA – Tumor-agnostic, TC – Thyroid Cancer, TTFI – Time to First Improvement, TTFW – Time to First Worsening

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